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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/524,531	03/13/2000	Beat Albert Imhof	PM 264679	7344

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EXAMINER	
ROARK, JESSICA H	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 02/06/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/524,531	Applicant(s) IMHOF ET AL.	
	Examiner Jessica H. Roark	Art Unit 1644	

-- The MAILING DATE of this c mmunication appears on the c ver sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 June 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) *3-9 and 14-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 10-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The Examiner of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Jessica Roark, Art Unit 1644, Technology 1600.

2. Applicant's election with traverse of Group I (Claims 1-2 and 10-13 directed to CRAM-1) in Paper No. 10 (filed 6/18/01) is acknowledged.

The traversal is on the grounds that the polynucleotide encoding and antibodies to the CRAM-1 polypeptide have been inappropriately segregated. This is not found persuasive because as set forth in Paper No. 7, these products are distinct as shown by their different structures and modes of action, and their different classification.

The requirement is still deemed proper and is therefore made FINAL.

Claims 3-9 and 14-19 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention.

Claims 1-2 and 10-13, as drawn to a CRAM-1 polypeptide, *are under consideration in the instant application.*

3. In order to facilitate the prosecution of this application, applicant is requested to cancel all non-elected embodiments from the claims (i.e., the CRAM-2 polypeptide of SEQ ID NO:14 in claims 1 and 12).

4. Sequence compliance: The CRF, paper copy of the Sequence Listing and Statement that the CRF and Sequence Listing are identical, filed 6/18/01, has been found acceptable in view of Applicant's comments of 11/7/01 pointing out support for the previously recited sequence in the originally filed Sequence Listing.

However,
5. The specification is objected to under 37 CFR 1.821(d) because the SEQ ID NOS are not disclosed in the specification adjacent all referenced sequences. Even after entry of the amendment filed 11/7/01 sequences lacking identifiers still appear at least on pages 3, 5, 9, 22 (2 sequences) and 33. Applicant is requested to carefully review the specification for additional sequences requiring sequence identifiers. Appropriate correction is required.

If these sequences are not presently included in the Sequence Listing, Applicant is reminded to provide a new Sequence Listing, CRF and Statement that the paper copy and CRF are identical.

6. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Europe on 3/11/99. It is noted, however, that applicant has not filed a certified copy of the EP 99200746.8 application as required by 35 U.S.C. 119(b).

In the absence of such documentation, any prior art identified under 35 USC 102(a) will be applied until such time as Applicant perfects the claim for foreign priority, assuming such documentation provides an adequate written description of the instant invention.

7. Applicant's IDS, filed 12/5/00 (Paper No. 5), is acknowledged.

8. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention *to which the claims are directed.*

9. Formal drawings have been submitted which fail to comply with 37 CFR 1.84.
Please see the enclosed form PTO-948.

10. INFORMATION ON HOW TO EFFECT DRAWING CHANGES

A. Correction of Informalities -- 37 CFR 1.85

New corrected drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings **MUST** be filed within the **THREE MONTH** shortened statutory period set for reply in the "Notice of Allowability." Extensions of time may NOT be obtained under the provisions of 37 CFR 1.136 for filing the corrected drawings after the mailing of a Notice of Allowability. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

B. Corrections other than Informalities Noted by Draftsperson on form PTO-948.

All changes to the drawings, other than informalities noted by the Draftsperson, **MUST** be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings **MUST** be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

Timing of Corrections

*Applicant is required to submit acceptable corrected drawings within the time period set in the Office action. See 37 CFR 1.185(a). Failure to take corrective action within the set (or extended) period will result in **ABANDONMENT** of the application.*

11. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which Applicant may become aware in the specification.

12. Claim 1 is objected to because of the following informalities: it appears that "isoalted" was intended to read -- isolated --. Appropriate correction is required.

13. Claim 10 is objected to because of the following informalities: the claim should begin with an article, e.g., "*A* soluble polypeptide". Appropriate correction is required.

14. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15. Claims 2 and 10-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "essentially" in claims 2, 10-13 is a relative term which renders the claims indefinite. The term "essentially" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is suggested that Applicant delete the term.

Applicant is reminded that any amendment must point to a basis in the specification so as not to add new matter. See MPEP 714.02 and 2163.06.

16. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

17. Claims 1-2 and 10-13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the amino acid sequences of SEQ ID NO:13 and SEQ ID NO:15 and certain fragments of these sequences as noted below; does not reasonably provide enablement for sequences that are "at least 70%" or "70% to *essentially* 100%" homologous; or for "at least part of the amino acid sequence". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification does not provide a sufficient enabling description of the claimed invention. Applicant has disclosed two amino acid sequence (SEQ ID NO:13 and SEQ ID NO:15) with a disclosed function of vascular adhesion and leukocyte transmigration (e.g., pages 25-28). The specification also identifies an extracellular region comprising the V and C2 domains, a transmembrane domain, and a cytoplasmic domain (e.g., Figure 8 and Brief Description of Figure 8 on page 9). A fusion protein comprising the fragment of the polypeptide ending with the sequence DGV (amino acids 289-291 of either SEQ ID NO:13 or SEQ ID NO:15) is also disclosed (e.g. page 17 of the specification in view of SEQ ID NO:13 and SEQ ID NO:15), as are fusion proteins comprising either the single Ig (V) domain or the two domains of the extracellular region (VC2) (e.g., bridging paragraph of pages 17-18).

However, the instant claims encompass in their breadth *any* polypeptide that is "at least 70%" or "70% to *essentially* 100%" homologous; or that is "at least part of the amino acid sequence". There does not appear to be sufficient guidance in the specification as filed as to how the skilled artisan would make and use these various polypeptides encompassed by the instant claims.

Homology: Attwood (Science 2000; 290:471-473) teaches that "[i]t is presumptuous to make functional assignments merely on the basis of some degree of similarity between sequences. Similarly, Skolnick et al. (Trends in Biotech. 2000; 18(1):34-39) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (e.g., "Abstract" and "Sequence-based approaches to function prediction", page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see in particular "Abstract" and Box 2).

For example, although Aurrand-Lions et al. (Blood 2001; 98:3699-3707) teach that the instant mouse and human polypeptides (which they call JAM-2) have homology to other molecules also shown to be involved in vascular adhesion (i.e., JAM-1 and JAM-3), the differences in the amino acid sequences between these molecules result in differences in expression and function with respect to their regulation of vascular permeability (see entire document, e.g., Abstract). Thus even though a comparison of JAMs indicates a similar overall structure as identified by the V, C2, transmembrane and cytoplasmic domains; the structural similarity and homology of the JAMs still does not permit the skilled artisan to identify which sequences or sequence fragments are essential for a particular function since the individual homologous JAMs have distinct functions.

In view of this unpredictability; the skilled artisan would not reasonably expect a polypeptide having anything less than 100% identity *over the full length of SEQ ID NO:13 or SEQ ID NO:15* to *share the same function* as the polypeptide of SEQ ID NO:13 or SEQ ID NO:15. The unpredictability that a particular function would be shared obviously increases as the shared identity decreases. Further, it is noted that the instant claim language requires only "homology" rather than identity; thus permitting even greater amino acid variation.

Thus the recitation of homology language, in the absence of *a testable function* and limitations regarding the *sequence length over which the homology is required*; does not allow the skilled artisan to make and use the polypeptides commensurate in scope with the instant claims without undue experimentation.

Polypeptide fragments: Although a fusion protein comprising the extracellular region was disclosed to inhibit transmigration (e.g. page 27 at lines 26-31), without detailed direction as to which amino acid sequences in the extracellular region are essential to this function, a person of skill in the art would not be able to determine without undue experimentation which of the plethora of polypeptide sequences "having at least a part" of the amino acid sequence would share this ability, including those that have only one of the two extracellular domains (claim 12). Neither would the skill artisan be able to make polypeptide sequences "having at least a part" of the amino acid sequence of the polypeptide that would mediate the disclosed function of vascular adhesion without extensive experimentation, since only full length polypeptides or a fusion protein comprising a nearly full-length polypeptide ending with the sequence DGV (amino acids 289-291 of either SEQ ID NO:13 or SEQ ID NO:15) are disclosed to have this function.

Other than those fragments identified clearly in the specification by both sequence length *and* associated function; a person of skill in the art would not know which other sequences are essential, which sequences are non-essential, and what particular sequence lengths identify essential sequences. Thus there is insufficient guidance to direct a person of skill in the art to select other undisclosed sequences or sequence lengths as essential for a function either of vascular adhesion, or soluble inhibitor.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. Without sufficient guidance, the changes which can be made in the instantly recited polypeptide sequences and still maintain the functional properties of the polypeptide of SEQ ID NO:13 or SEQ ID NO:15 are unpredictable, as is the identity of which sequence fragments would encode a functional polypeptide; thus the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

It is suggested that Applicant limit the claims to polypeptides having only limited variation (e.g. 100% homology) *over the full length of the sequence,* and *possessing testable functional activity*; and to those polypeptide fragments clearly identified in the specification as encompassing a testable functional activity.

Applicant is reminded that any amendment must point to a basis in the specification so as not to add new matter. See MPEP 714.02 and 2163.06.

18. Claims 1-2 and 10-13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The following written description rejection is set forth herein.

The instant claims are drawn to a genus of polypeptides having at least 70% homology to the polypeptides of SEQ ID NOS: 13 or 15 or having "at least a part" of these amino acid sequences. The instant claims do not require that this genus of polypeptides share a testable function.

The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 3rd column).

Applicant has disclosed two amino acid sequences (SEQ ID NO:13 and SEQ ID NO:15) and a fusion protein comprising a nearly full-length polypeptide ending with the sequence DGV (amino acids 289-291 of either SEQ ID NO:13 or SEQ ID NO:15) which are able to mediate leukocyte transmigration of vascular endothelium (e.g., pages 25-28). A fusion protein comprising the extracellular region was also disclosed to inhibit transmigration (e.g. page 27 at lines 26-31).

However, the genus of polypeptides with various percentage of homology to SEQ ID NOS:13 or 15 or subsequences thereof is very large; and a great deal of variability is encompassed by the instant claims. However, that claims are not limited to polypeptides sharing a disclosed function. Neither has Applicant disclosed, nor does the art recognize, the requisite structural features of the polypeptides which results in the disclosed functional activities, a feature deemed essential to the instant invention. Therefore, one of skill in the art would not recognize Applicant to be in possession of the genus of polypeptides as encompassed by the instant claims.

Consequently, the claimed invention is not described in such a way as to reasonably convey to one of ordinary skill in the art that the inventor, at the time the application was filed, had possession of the invention. See Regents of the University of California v. Eli Lilly & Co., 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). Applicant is also directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicant is invited to point to clear support or specific examples of the claimed invention in the specification as-filed.

19. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

20. Claims 1-2, 10-11 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Dumas Milne Edwards et al. (WO 99/06551).

Dumas Milne Edwards et al. teach the polypeptide of SEQ ID NO:294 and methods for expressing and isolating this polypeptide (see pages 1-13, 114 and 253).

The polypeptide of Dumas Milne Edwards et al. comprises an amino acid sequence that is 100% identical to SEQ ID NO:15 over residues 1-89 and shows at least 70% sequence homology over at least part of SEQ ID NO:13. In addition, the polypeptide of Dumas Milne Edwards et al. would inherently be soluble since it does not encompass a transmembrane domain.

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the polypeptide of SEQ ID NO:294 taught by Dumas Milne Edwards et al. In addition, the intended uses of the polypeptides do not carry patentable weight per se and the claims read on the active or essential ingredient of the polypeptide.

21. No claim is allowed.

22. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jessica Roark, whose telephone number is (703) 605-1209. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Jessica Roark, Ph.D.
Patent Examiner
Technology Center 1600
February 5, 2002

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2/6/02